REMARKS

Upon entry of the present amendment, claims 1-15 are pending in the application.

Formal Matters

The Examiner has objected to the drawings because the titles in Figures 3 and 6 contain words that have been misspelled. A proposed title of drawing correction have been submitted in the amendment above, according to Examiner's suggestion. Applicants wish to delay formal correction of these drawings until after the Examiner has considered the proposed title of the drawing correction. Thus, Applicants submit that this objection has been overcome.

Rejections under 35 USC 112, second paragraph

Claims 1-15 stand rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regards as the invention. In response, Applicants have amended claims 1, 7 and 11 as decribed below.

Claims 1-10 were considered indefinite by the Examiner because in claim 1 it was unclear whether the method for identifying, classifying, or quantifying nucleic acids includes or does not include a sequencing step. Claim 1 has been amended to include "without sequencing" in its preamble. Thus, Applicants submit that claim 1 has been rendered definite.

Claims 11-15 were considered indefinite by the Examiner because in claim 11 it was unclear whether the method for extending the sequence in a length-subsequence combination of nucleic acids included or did not include a sequencing step. Claim 11 has been amended to include "without sequencing" in its preamble. Thus, Applicants submit that claim 11 has been rendered definite.

Claim 7 was considered indefinite by the Examiner because it was unclear whether the "sequencing step" referred to performing this step before or after the nucleotide database step. Claim 7 has been amended to specify that the step be done "after steps (b) or (d)". Therefore, it would be done before the nucleotide database step. The Examiner also alleges that claim 7 is indefinite because it does not specify if traditional sequencing is used, or a non-traditional sequencing method.

Applicants assert that use of "sequencing" in claim 7 is definite. The instant use of sequencing would encompass any method that is known in the art and could be used to sequence a nucleic acid. This would include both traditional and non-traditional sequencing techniques.

MPEP 2173.04 states "If the scope of the subject matter embraced by the claims is clear, and if the applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 USC 112, second paragraph." Applicants assert that the scope of claim 7, as amended, is clear. Thus, Applicants submit that claim 7, as amended is definite.

Applicants submit that with the above amendments, all claims are definite. Therefore, Applicants request that this rejection be withdrawn.

Rejections under 35 USC 102(b)

Claims 1 and 6-11, stand rejected, as being anticipated by Rothberg *et al.* WO 97/15690 published May 1, 1997 ("WO 97/15690"). Applicants traverse for reasons detailed below.

The Examiner alleges that WO 97/15690 contains all of the constraints of claims 1 and 6-11. On page 3, lines 18-22 of the Office action, Examiner states "Claims 1 & 6-10 are drawn to a method for identifying, classifying, or quantifying nucleic acids with different nucleotide sequences in a sample, comprise probing sample with a recognition means, generating a first signal that represents the length and identity of the target subsequences in the targeted nucleic acid, selecting a targeted nucleic acid, [and] *extending the sequence information under conditions that generate a second signal...*" (Emphasis added). This limitation of claim 1 is not found in the description of the teachings of WO 97/15690 found on page 4 of the Office action, which only teaches the use of the first round of signal generation using the unextended recognition means.

WO 97/15690 only teaches the generation of the first signal. It does not teach the extension of the recognition means stipulated in claim 1.

The instant invention comprises a method in which after the methods described in WO 97/15690 are used, the recognition means are extended and a second signal is generated. The recognition means recognizes a different target nucleotide subsequence. When the recognition means is extended, more information is added to the recognition means to make it more specific. In one embodiment of the invention, a recognition means would be a primer that hybridized to a

certain target sequence. Extensions of this recognition means could be undertaken by adding another nucleotide to the 5' or 3' end. This would limit the target sequences it would hybridize to, theoretically, by 75%. This way the second signal generated by this extended recognition means would represent fewer target sequences.

The Examiner does mention one type of extension in relation to WO 97/15690 in the Office action on page 4, lines 12-14. "They teach extending the target sequences with a DNA polymerase in order to generate another signal that has the same length and the same identity as the target subsequence." This teaches the use of a polymerase to copy or amplify a target sequence. It does not teach the extension and recognition means as described above.

For a reference to anticipate a claim, it must teach every aspect of the claimed invention either explicitly or impliedly. This extended recognition means/second signal stipulation is not taught or mentioned by WO 97/15690. Thus, Applicants request that this rejection be withdrawn insofar as it applied to claims 1, and 6-10.

Claim 11 also stands rejected as being anticipated by WO 97/15690. Applicants traverse for the reasons detailed below.

As with claim 1, claim 11 teaches the use of extended recognition means to generate second signals that extend sequence information above and beyond the methods taught in WO 97/15690. Also, the extension mentioned is not the extension as described on page 16, lines 19-37 of WO 97/15690. Thus, WO 97/15690 does not anticipate claim 11 because it does not teach every aspect of the claimed invention. Applicants request that this rejection be withdrawn.

Rejections under 35 USC 103(a)

Claims 2-5 and 12-15 stand rejected for obviousness as being unpatentable over WO 97/15690 in view of WO 99/07896. Applicants traverse for reasons detailed below.

Examiner asserts that the combination of WO 97/15690 and WO 99/07896 would have made the subject matter of the rejected claims obvious at the time of the invention was made to one of ordinary skill in the art. Examiner alleges that WO 97/15690 teaches all the limitations of independent claims 1 and 11 as detailed above. Examiner also alleges that WO 99/07896 teaches the limitations introduced by dependent claims 2-5 and 12-15. However, as asserted above, WO 97/15690 does not teach all the limitations of independent claims 1 and 11.

WO 99/07896 teaches the use of an oligo-poisoning signal. It teaches unlabeled "poisoning" using primers. It teaches that this technique can be used to acquire increased

resolution. It does not teach the use of the extended recognition means, and does not teach the generation of a second signal. As explained above, WO 97/15690 does not teach this limitation either. The invention as claimed would not have been obvious to one of ordinary skill in the art because not all of the stipulations of these claims are taught by the prior art. Thus, Applicants request that this rejection be withdrawn.

CONCLUSION

Applicants submit that the application is in condition for allowance and such action is respectfully requested.

Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

The Commissioner is hereby authorized to charge any fees due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 15966-632 (Cura-132).

Respectfully submitted,

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Marked Up Version Showing Changes

In the claims:

Amend claim 1 as shown below:

1. (Amended) A method for identifying, classifying or quantifying one or more nucleic acids in a sample comprising a plurality of nucleic acids having different nucleotide sequences without sequencing, the method comprising:

(d) probing said sample with one or more recognition means wherein each recognition means recognizes a different target nucleotide subsequence or a different set of target nucleotide subsequences to provide one or more targeted nucleic acids;

(e) generating one or more first signals from said sample probed by said recognition means, each generated first signal arising from a targeted nucleic acid in said sample and comprising a representation of (*i*) the length between occurrences of target subsequences in said targeted nucleic acid, and (*ii*) the identities of said target subsequences in said targeted nucleic acid or identities of said target subsequences among which are included the target subsequences in said targeted nucleic acid;

(f) selecting one or more targeted nucleic acids based on their corresponding first signals;

(d) extending sequence information from one or more target subsequences in said selected targeted nucleic acid by one or more nucleotides providing one or more extended subsequences under conditions that generate one or more second signals arising from said selected targeted nucleic acid, at least one of whose subsequences has been extended, in said sample, wherein said second signal comprises a representation of (*i*) the length between occurrences of target subsequences, at least one of which has been extended, in said nucleic acid, and (*ii*) the identities of said selected target subsequences, at least one of which has been extended, in said selected targeted nucleic acid or identities of said target subsequences, at least one of which has been extended, among which are included the target subsequences in said selected targeted nucleic acid; and

(e). searching a nucleotide sequence database to determine sequences that match or the absence of any sequences that match one or more or of said selected targeted nucleic acids having at least one extended subsequence and represented by said generated second

signals, said database comprising a plurality of known nucleotide sequences of nucleic acids that may be present in the sample, wherein a sequence from said database is determined to match said selected targeted nucleic acid providing a generated second signal when the sequence from said database has both (*i*) the same length between occurrences of target subsequences, at least one of which has been extended, as is represented by the generated signal, and (*ii*) the same target subsequences, at least one of which has been extended, as are represented by the generated signal, or target subsequences, at least one of which has been extended, that are members of the same sets of target subsequences represented by the generated signal,

whereby a matched nucleic acid in said sample is identified, classified, or quantified.

Amend claim 7 as shown below:

7. (Amended) The method of claim 1 wherein said method additionally includes

recovering a fragment of a nucleic acid in the sample which generates said signal <u>after steps (b) or (d)</u>;

sequencing said fragment to determine at least a partial sequence for said fragment; and

verifying that said sample comprises a nucleic acid having a sequence comprising at least a portion of said determined sequence.

Amend claim 11 as shown below:

11. (Amended) A method for extending the sequence in a length-subsequence combination of one or more nucleic acids in a sample comprising a plurality of nucleic acids having different nucleotide sequences <u>without sequencing</u>, said method comprising:

(a) probing said sample with one or more recognition means wherein each recognition means recognizes a different target nucleotide subsequence or a different set of target nucleotide subsequences to provide one or more targeted nucleic acids;

(b) generating one or more first signals from said sample probed by said recognition means, each generated first signal arising from a targeted nucleic acid in said sample and

comprising a representation of (*i*) the length between occurrences of target subsequences in said targeted nucleic acid, and (*ii*) the identities of said target subsequences in said targeted nucleic acid or identities of said target subsequences among which are included the target subsequences in said targeted nucleic acid;

(c) selecting one or more targeted nucleic acids based on their corresponding first signals; and

(d) extending sequence information from one or more target subsequences in said targeted nucleic acid by one or more nucleotides providing one or more extended subsequences under conditions that generate one or more second signals arising from selected targeted nucleic acid in said sample at least one of whose subsequences has been extended, wherein said second signal comprises a representation of (*i*) the length between occurrences of target subsequences, at least one of which has been extended, in said nucleic acid, and (*ii*) the identities of said target subsequences, at least one of which has been extended, in said selected targeted nucleic acid or identities of said target subsequences, at least one of which has been extended, among which are included the target subsequences in said selected targeted nucleic acid;

whereby a matched nucleic acid in said sample has an extended sequence in said length-subsequence combination.

In the drawings:

In Figure 3, amend the title as follows:

"FIG. 3. Oligo-competition set up. Oligo-competition primers are set up on the J or R side based on the predicted sequence of the GeneCalled™ fragment. Oligo-competition reactions involve J23 and R23 primer[e]s with a fifty fold excess of the oligo-competition primers."

In Figure 6, amend the title as follows:

"FIG. 6. Example of id[n]entification of the first base on the 3' side of the restriction enzyme sites on the R and J side for each QEA peak in the BsphI and BglII double digest of rat liver cDNA. (see text for details)"